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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/804,369 | 03/12/2001 | Bastiaan Driehuys | 5770-21 | 9041 |

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| EXAMINER | |
|---|---|
| HARTLEY, MICHAEL G | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1616 | 9 |

DATE MAILED: 12/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/804,369 | Applicant(s) DRIEHUYS ET AL. | |
|---|---|---|---|
| | Examiner Michael G. Hartley | Art Unit 1616 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3-23 and 89-102* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-19,22,23,89-91, 94-97 and 100-102* is/are rejected.

7)☒ Claim(s) *20,21,92,93,98 and 99* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

### *Response to Amendment*

The amendment filed 11/07/2002 has been entered. Claim 2 has been canceled. Claims 1, 9 and 20 have been amended. New claims 89-102 have been added.

### *Response to Arguments*

Any previous rejections that have not been reiterated herein have been withdrawn.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-19, 89-91, 94-97 and 100-102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Albert (US 5,545,396), by itself, and/or in view of Brasch (US 5,811,076), for the reasons set forth in the office action mailed 8/16/2002.

Applicant's arguments filed 11/07/2002 have been fully considered but they are not persuasive.

Applicant asserts that Albert fails to disclose injecting the quantity of gaseous $^{129}Xe$ into the subject as set forth in the claims.

Albert discloses that the preferred method includes intravenous injection of the hyperpolarized gas, e.g., $^{129}Xe$, as set forth in column 12, lines 44-55. Albert teaches that the amount is an imageable amount which is administered, see column 3, lines 45-56. While Albert does not specifically disclose this amount in cc for intravenous administration (as claimed), such an amount would be dependent upon the size of the subject and would be optimized thereby. Note Albert teaches that the subject may be animal or human (see claim 26). Therefore, one of ordinary skill in the art would have recognized that the imageable amount is an amount which is to be optimized depending on various factors, i.e., size of the subject, as well as, purity of the $^{129}Xe$ sample, etc. Generally, differences in concentration (e.g., such as an amount) will not support the patentability of subject matter encompassed by the prior art unless there

is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See also In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969), *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Since the amount of $^{129}$Xe taught by Albert is an imageable amount, clearly Albert recognized this as a result-effective variable to achieve a recognized result, i.e., imaging of the pulmonary system, and one that was to be optimized by routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).

Applicant also asserts that Albert fails to teach the inherent characteristics of the invention, such as, injection rates, sequential administrations, etc.

This assertion is not on point because only the functional limitations were stated as being inherent characteristics, these include the limitations, such as, that the gas travels along a portion of the pulmonary circulation after delivery (i.e., claim 7), remains in the blood stream (claim 10), MRI signals overlap (claim 12), etc. Albert does disclose methods of delivery which include controlled rate delivery (i.e., the gas may be provided by continuous, discontinuous, and/or quasi-continuous modes, see column 14, lines 10-33 and column 4, lines 54+, as claimed in new claim 100). Also Albert teaches that the both inhalation and intravenous routes of delivery may be used (column 12, lines 44-55) with separate routes and/or separate times of administration, which would encompass delivery of by both intravenous and inhalation combined as claimed and at separate times.

Applicant asserts that Brasch does not resolve the deficiencies of Albert.

This is not found persuasive because Albert discloses methods of MRI imaging the pulmonary system by the intravenous administration of an imageable amount of hyperpolarized $^{129}$Xe, but does not specifically disclose this includes imaging pulmonary embolism. Brasch is only relied upon to teach that MRI is an imaging modality which is used to image pulmonary embolism, thus, one of ordinary skill in the art would have been motivated to employ the pulmonary imaging methods disclosed by Albert to include

detection of embolism to provide important clinical information, as taught by Brasch. Also imaging techniques are commonly applied to both detect a condition and to monitor a therapy, i.e., in a clinical setting as suggested by both Albert, e.g., column 17 and Brasch, column 1. The newly added claims rejected herein do not differentiate over the cited art, as these claims relate to limitations previously stated and/or readdressed herein, such as, optimizing the amount of administration (e.g., for humans, etc.), evaluating treatment (i.e., which is a main reason for imaging in a clinical setting), the use of both intravenous and inhalation delivery (Albert teaches both and combination thereof), controlled rate delivery (e.g., quasi-controlled delivery, as disclosed by Albert), etc. Also, none of these limitations have been expressly asserted for differentiation over the cited art.

Claims 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Albert (US 5,545,396), by itself and/or in view of Brasch (US 5,811,076) as applied to claims 1 and 3-19 above, and further in view of Unger (US 6,315,981), for the reasons set forth in the office action mailed 8/16/2002.

Applicant asserts that Unger fails to disclose the direct injection of gaseous $^{129}Xe$.

This is not found persuasive because the liposome compositions disclosed by Unger are gas-filled microspheres or gas-filled liposomes, wherein the gas includes hyperpolarized gas. Thus, while the liposome compositions may be in an aqueous carrier, gas is being administered. The claims are not limited to administering gas, by itself, but would encompass gas which contained in some type of carrier, as disclosed by Unger. Further, Unger is being relied upon teaching expelling larger bubbles to yield gasbubbles which are under 12 microns, which encompasses the claimed range, see column 9, lines 65+, as large bubbles may be detrimental for intravenous use because they can cause an embolism.

***Allowable Subject Matter***

Claims 20, 21, 92, 93, 98 and 99 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. While Unger teaches encapsulating a gas in a surfactant, Unger fails to teach or suggest a further step of introducing a surfactant into a subject proximate to the injection site of a

hyperpolarized gas, as well as, the methods of preparing the hyperpolarized gas prior to administration as claimed, and the limitations set forth in new claims 92, 93, 98 and 99.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (703) 308-4411. The examiner can normally be reached on M-F, 7:30-5, off alternative Mondays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose G. Dees can be reached on (703) 308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

MH
December 18, 2002

MICHAEL G. HARTLEY
PRIMARY EXAMINER